

# PATENT COOPERATION TREATY

From the  
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

PCT

REC'D 31 MAY 2005

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## WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY (PCT Rule 43bis.1)

Date of mailing  
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference  
see form PCT/ISA/220

**FOR FURTHER ACTION**  
See paragraph 2 below

International application No.  
PCT/US2005/005418

International filing date (day/month/year)  
18.02.2005

Priority date (day/month/year)  
25.02.2004

International Patent Classification (IPC) or both national classification and IPC  
C07D223/16, C07D401/12, C07D417/12, C07D413/12, C07D403/12, C07D409/12, C07D405/12, C07D413/14,

Applicant  
ELI LILLY AND COMPANY

### 1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☒ Box No. VIII Certain observations on the international application

### 2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

### 3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:



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**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY**

International application No.  
PCT/US2005/005418

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**Box No. I Basis of the opinion**

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1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
  - ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
  - a. type of material:
    - ☐ a sequence listing
    - ☐ table(s) related to the sequence listing
  - b. format of material:
    - ☐ in written format
    - ☐ in computer readable form
  - c. time of filing/furnishing:
    - ☐ contained in the international application as filed.
    - ☐ filed together with the international application in computer readable form.
    - ☐ furnished subsequently to this Authority for the purposes of search.
3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

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**Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application,  
☒ claims Nos. 18-25 (with respect to industrial applicability)

because:

- ☒ the said international application, or the said claims Nos. 18-25 relate to the following subject matter which does not require an international preliminary examination (*specify*):

**see separate sheet**

- ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):
- ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
- ☐ no international search report has been established for the whole application or for said claims Nos.
- ☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:
- |                            |  |
|----------------------------|--|
| the written form           | <input type="checkbox"/> has not been furnished            |
|                            | <input type="checkbox"/> does not comply with the standard |
| the computer readable form | <input type="checkbox"/> has not been furnished            |
|                            | <input type="checkbox"/> does not comply with the standard |
- ☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-bis of the Administrative Instructions.
- ☐ See separate sheet for further details

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**Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

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1. Statement

Novelty (N)	Yes: Claims	
	No: Claims	1-37
Inventive step (IS)	Yes: Claims	
	No: Claims	1-37
Industrial applicability (IA)	Yes: Claims	1-17,26-37
	No: Claims	

2. Citations and explanations

**see separate sheet**

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**Box No. VIII Certain observations on the international application**

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The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

**see separate sheet**

**Re Item III**

**Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

Claims 18-25 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I) PCT).

**Re Item V**

**Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

Reference is made to the following documents:

D1: WO 93/04686 A (SMITHKLINE BEECHAM CORPORATION) 18 March 1993  
(1993-03-18)

D2: US-A-4 265 890 (HOLDEN ET AL) 5 May 1981 (1981-05-05)

D3: WO 93/03015 A (SMITHKLINE BEECHAM CORPORATION) 18 February 1993  
(1993-02-18)

D4: KILPATRICK, ANDREW T. ET AL: "The .alpha.2-adrenoceptor antagonist SK & F 104078 has high affinity for 5-HT1A and 5-HT2 receptors" EUROPEAN JOURNAL OF PHARMACOLOGY , 166(2), 315-18 CODEN: EJPHAZ; ISSN: 0014-2999, 1989, XP002328505

**V.1. Novelty:**

The present application does not meet the criteria of Article 33(1) PCT, because the subject-matter of claims 1-37 is not new in the sense of Article 33(2) PCT:

Document D1 discloses compounds falling within the scope of present formula I in which R6 represents -OR<sup>12</sup> and which are useful for the treatment of depression and obesity (see International Search Report for details on citations). Therefore, the subject-matter of claims 1-37 is not novel (Article 33(2) PCT).

Example 19 of D2 is covered by the present general formula I when R3 represents methyl, R6 represents 4-F-phenyl-S- and R9 represents Cl. Therefore, the subject-matter of claims 1-16 is not novel (Article 33(2) PCT).

**V.2. Inventive Step:**

The present application does not meet the criteria of Article 33(1) PCT, because the subject-matter of claims 1-37, in as far as novel, does not involve an inventive step in the sense of Article 33(3) PCT:

Documents D1 and D3 disclose general formulae which overlap with the present formula I. The compounds of D1 and D3 are adrenergic antagonists and useful for the treatment of depression and obesity. The compounds described in D3 are actually excluded from the present general formula I by means of the proviso e) of claim 1.

Even though the compounds of D1 and D3 are characterized as  $\alpha$ -adrenoceptor antagonists, whereas the present compounds embody 5-HT<sub>2C</sub> receptor agonists, it is known from D4 that the benzazepine derivative SK&F 104078 which is in principle an  $\alpha_2$ -adrenoceptor antagonist, has high affinity for 5-HT<sub>2</sub> receptors.

In view of the teaching of the prior art, it would have been obvious to the skilled person to associate the formulae of D1 and D3 with a 5-HT<sub>2</sub> receptor activity, and to choose among said formulae when looking for further compounds for the treatment of obesity and neurological disorders such as depression.

Consequently, the subject-matter of claims 1-37 cannot be considered as involving an inventive step (Article 33(3) PCT).

**V.3. Industrial Applicability:**

The present application relates to compounds which are useful for the treatment of obesity, obsessive compulsive disorder, depression and anxiety and the subject matter of claims 1-17, 26-37 is therefore considered as industrially applicable (Article 33(4) PCT).

For the assessment of the present claims 18-25 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

**Re Item VIII**

**Certain observations on the international application**

The proviso d) of present claim 1 refers to R<sup>7</sup> and R<sup>8</sup> being each -OH. However, the definitions given for R<sup>7</sup> and R<sup>8</sup> in claim 1 does not include -OH, thereby rendering the definition of the subject-matter of the claims unclear (Article 6 PCT).